**DEPARTMENT OF HEALTH & HUMAN SERVICES** Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-386/S-026
NDA 20-387/S-022

Merck and Co., Inc.
Attention: Michael C. Elia, Ph.D.
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

24 AUG 2001

Dear Dr. Elia:

Please refer to your supplemental new drug applications dated July 24, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cozaar (losartan potassium) 25, 50, and 100 mg Tablets, and Hyzaar (losartan potassium/hydrochlorothiazide) 50-12.5 and 100-25 Tablets.

These "Changes Being Effected" supplemental new drug applications provide for final printed labeling revised as follows:

NDA 20-386

Under **ADVERSE REACTIONS**, Post-Marketing Experience, Hypersensitivity subsection, the sentence "Vasculitis, including Henoch-Schoenlein purpura, has been reported" has been added. It now reads as follows:

**ADVERSE REACTIONS,** Post-Marketing Experience, Hypersensitivity:
Angioedema, including swelling of the larynx and glottis, causing airway obstruction and/or swelling of the face, lips, pharynx, and/or tongue has been reported rarely in patients treated with losartan; some of these patients previously experienced angioedema with other drugs including ACE inhibitors. Vasculitis, including Henoch-Schoenlein purpura, has been reported. Anaphylactic reactions have been reported.

NDA 20-387

Under **ADVERSE REACTIONS**, Post-Marketing Experience, Hypersensitivity subsection, the sentence "Vasculitis, including Henoch-Schoenlein purpura, has been reported with losartan" has been added. It now reads as follows:

**ADVERSE REACTIONS,** Post-Marketing Experience, Hypersensitivity: Angioedema, including swelling of the larynx and glottis, causing airway obstruction and/or swelling of the face, lips, pharynx, and/or tongue has been reported rarely in patients treated with losartan; some of these patients previously experienced angioedema with other drugs including ACE inhibitors. Vasculitis, including Henoch-Schoenlein purpura, has been reported with losartan. Anaphylactic reactions have been reported.

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the included final printed labeling (package insert included in your submissions of July 24, 2001). Accordingly, these supplemental applications are approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5313

Sincerely,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research